

# The ECOTOXicology Knowledgebase Literature Search and Review Processes for Identifying and Curating Toxicity Data for Ecological Risk Assessments

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The views expressed in this presentation are those of the authors and do not necessarily reflect the views or policies of the U.S. EPA.

### **Outline**

- Background and History of the ECOTOX Knowledgebase
- ECOTOX Pipeline: Literature Search, Systematic Review, and Data Curation
- Applications and Tools using Data from ECOTOX
- Summary

### The Challenge

- Risk assessors needed a cost-effective means of locating relevant ecological toxicity data for:
  - Prioritizing chemical cleanup at hazardous waste sites
  - Assisting in the assessment of potential hazards of pollutants through the Clean Air Act, the Clean Water Act, the Federal Insecticide, Fungicide and Rodenticide Act and the Toxic Substances Control Act.
- Data must be identified with transparent processes and be accessible
- Duplicative efforts for data gathering wastes resources across state and federal agencies

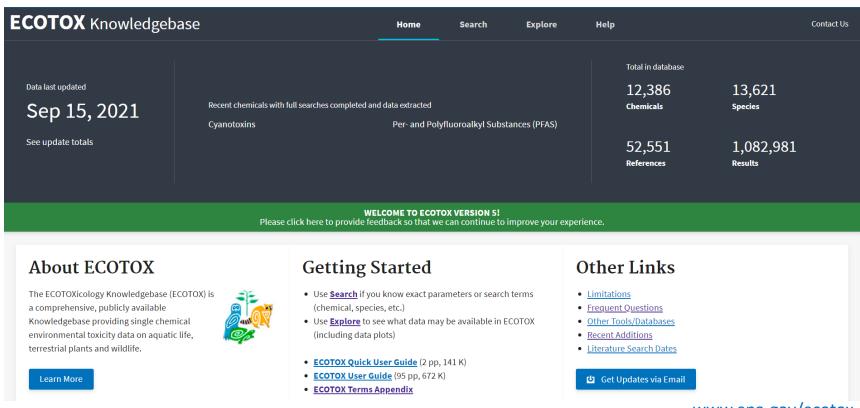
### The On-going Challenge and Opportunities

- The accelerated pace of chemical risk assessment for ecological receptors
- Discovery of "new" chemicals of ecotoxicological concern
- Increase in number and diversity of journals
- Changing landscape of toxicity data used for ERA
- Decreasing dependency of traditional whole animal testing for ERA

- Tool development to:
  - Expedite information gathering of information
  - Rapidly sort through BROAD keyword searches (e.g., chemical name)
- Digital formats of journals allow for use of data analytic applications
- Shift from apical endpoints to NAMs requires transparent development of controlled vocabulary for systematic data curation
- Providing a means to take full advantage of existing data before conducting new toxicity studies

### What is the ECOTOXicology Knowledgebase?

- 30+ years of curating single chemical toxicity effects data for aquatic and terrestrial organisms
- Systematic and transparent literature search and review of open and grey literature
- >1 million test results from >52,000 references



#### **ECOTOX Data Curation Pipeline**

chemical verification & development of search terms

Conduct literature searches

Identify and acquire potentially applicable studies

Review literature for applicability

Extract study and toxicity data



www.epa.gov/ecotox

Chemical verification & development of search terms

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- Verify CASRN
- Search various sources for chemical term
- Synonyms
- Eliminate poor search terms

Tak(Acilid OR Albrass OR Bexton OR "CP 31393" OR "Kartex A" OR Muharicid OR Niticid OR Propachlor OR Propachlore OR Ramrod OR Satecid OR "US EPA PC Code 019101")

\* Web-based tool to identify and document relevant search terms

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#### **Chemical-based Literature Searches**

#### **Search Engines**

- 1. Scopus/Science Direct
- 2. ProQuest
- 3. Web of Science
- 4. PubAg/AGRICOLA
- 5. PubMed Toxline/TOXNET
- 6. Dissertation Abstracts

\* Semi-automated batch searches with Abstract Sifter Plus



Chemical verification & development of search terms

Conduct literature searches

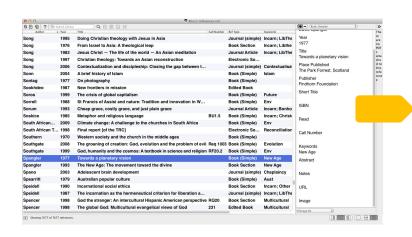
**Identify and** acquire potentially applicable studies

Review literature for applicability

**Extract study** and toxicity data



#### Literature Search Results



#### Title and **Abstract** Screening

sulfur Dust Bag: A Novel Technique for Ectoparasite control in Poultry System

DOI: 10.1093/jee/tow146

#### **Full Text** Screening

The impact of the Cyanamid Canada Co. discharges to benthic invertebrates in the Welland River in Niagara Falls, Canada

MIKE DICKMAN and GRAZVNA RVGIEL

Biological Sciences Department, Brock University, St. Catharines, Ontario, Canada L2S 3A

In 1986, the International Joint Commission (IJC) recommended that the Ningara River watershed should be declared in Area of Concern (AGC). This IJC recommendation was raified by the declared in Area of Concern (AGC). This IJC recommendation was raified by the declared in Area of Concern (AGC) and IJC recommendation was raified by the AGC and IJC recommendation was raified by the AGC and IJC recommendation and IJC recommendation projects that permit uses that were previously impaired. To this end we attempted to determine whether or not the sedemine at 7 may into sear the Cyanamid Canada (Chemical) Concernation was the Cyanamid Canada (Chemical) Concernation and the Individual Concernation of the Individual Concernation of the Cyanamid Canada (Chemical) Concentration was the Cyanamid Canada (Chemical) Concernation and the Individual Concernation of the Cyanamid Canada (Chemical) Concernation (Chemical) Chemical Ch

ran (e.g., sludge worms constituted 68% of all the organisms collected). The lowest chiracomois ensities were observed at stations 1, 2, and 4, which were the only stations situated close to personner were otherweal as stations 1, 2, and 4, wante were time only stations situated close typanamid's discharge pipes. The absence, of clams and mayfiles which burrow to greater depth than do chironomids and studge worms, probably reflects the inability of the deeper dwellin burrowers to tolerate the contaminants which we recorded at these 3 stations. The absence of a rustaceans from these same 3 stations (stations 1, 2 and 4) when coupled with their low bio

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### **Applicability Requirements**

Identify and acquire potentially applicable studies

Review literature for applicability

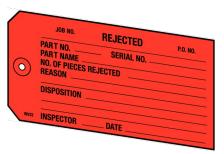
	Key Area	Data Requirement	applicable studies
P (Population)	Species	<ul> <li>Taxonomically verifiable organisms         (including cells, organs, gametes, embryos, plant cuttings)         [NOT bacteria, humans, monkeys, viruses, or yeast]</li> </ul>	
E (Exposure)	Chemical	Single, verifiable chemical toxicants, administered through an acceptable route.	
	Exposure Amount (Concentration)	<ul> <li>Exposure amount is quantified, either as a concentration in the environment when administered via soil or water, or as a dosage when introduced directly into or on the organism, via injection, orally, or topically.</li> </ul>	
	Exposure Duration	<ul> <li>Known duration from the time of initial time of measurement.</li> </ul>	exposure to the
C (Comparator/Control)	Control	Must have a control treatment <sup>a</sup>	
O (Outcome)	Effect	<ul><li>Biological effect measured</li><li>Effect concurrent with associated chem</li></ul>	ical exposure
	Publication Type	<ul> <li>Primary source of the data</li> <li>Study must be a full article in English</li> <li>[NOT: Review article or abstract citation</li> </ul>	n only]

### **Exclusion Documentation**

#### All Excluded and Non-Applicable studies are Tagged with the reason for rejection

- Abstract published as an abstract
- Bacteria only test organism is a bacteria
- CAS # Unavailable could not verify/locate chemical CAS Registry number
- Chemical method description of chemical analysis procedures
- Fate only report chemical distribution in media
- Human Health data on human subjects of surrogate animal subjects for human health risk assessment
- Incident reports death of animal by poison, but does not provide concentration/duration of exposure
- Method paper only reports methods for conducting a toxicity test or other aspect of an experiment
- Mixture paper reports results from mixture of chemicals; no single chemical exposure results
- Modeling results of the development of a model; no primary data available

- No Conc the authors report a response in an organism but do not provide conc/dose/app rate
- No Duration duration of exposure is not presented
- No Effect paper does not report observed responses adverse of otherwise
- No Toxicant (ozone, CO2)
- Non-English
- Nutrient in situ chemical tested as nutrient
- PUBL AS duplicate data published elsewhere
- Retracted paper retracted by Journal
- Review primary data published elsewhere
- Sediment only sediment concentration presented
- Survey chemical measured in organism, but lack quantification of exposure (dose/duration)
- Virus virus is only test organism
- Yeast yeast is only test organism



Chemical verification & development of search terms

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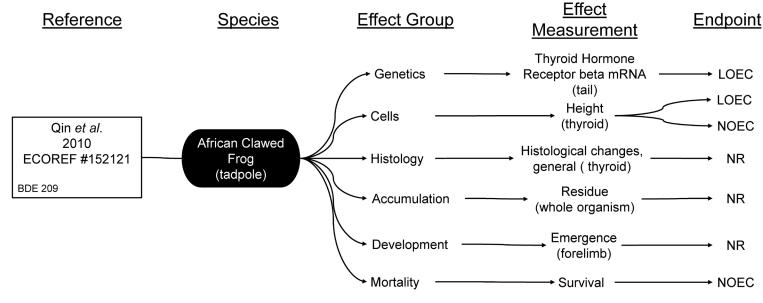




Journal of Environmental Sciences
Volume 22, Issue 5, 2010, Pages 744-751



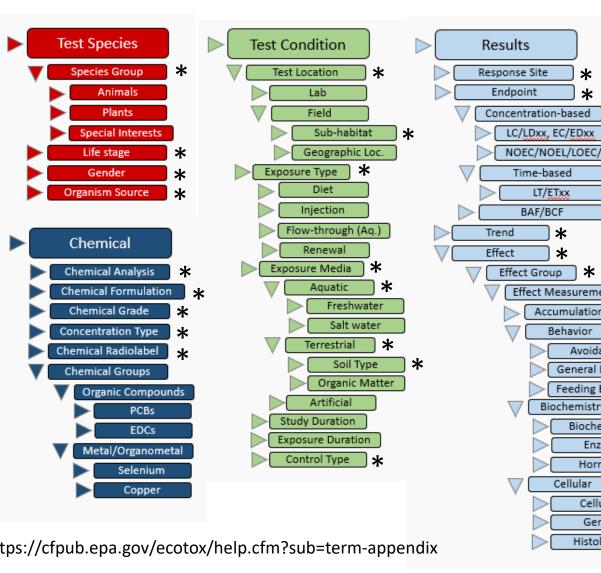
Thyroid disruption by technical decabromodiphenyl ether (DE-83R) at low concentrations in *Xenopus laevis* 



NOEC = No Observed Effect Level LOEC = Lowest Observed Effect Level NR = Not Reported

### **ECOTOX Data Fields**

**Unique Identifiers** Chemical ID **CASRN DTXSID** Taxonomic ID NCBI TaxID **ITIS TSN** 



**Extract study** and toxicity data

\*

\*

\*

\*

LC/LDxx, EC/EDxx

Time-based

BAF/BCF

LT/ETxx

\*

Effect Measurement

Accumulation

Behavior

\*

Avoidance

General Behavior

Feeding Behavior

Biochemical

Enzyme

Hormone

Cellular

Genetic

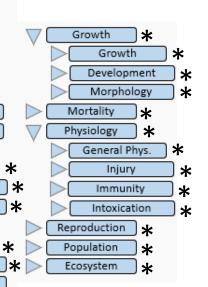
Histological

Biochemistry ] \*

Cellular

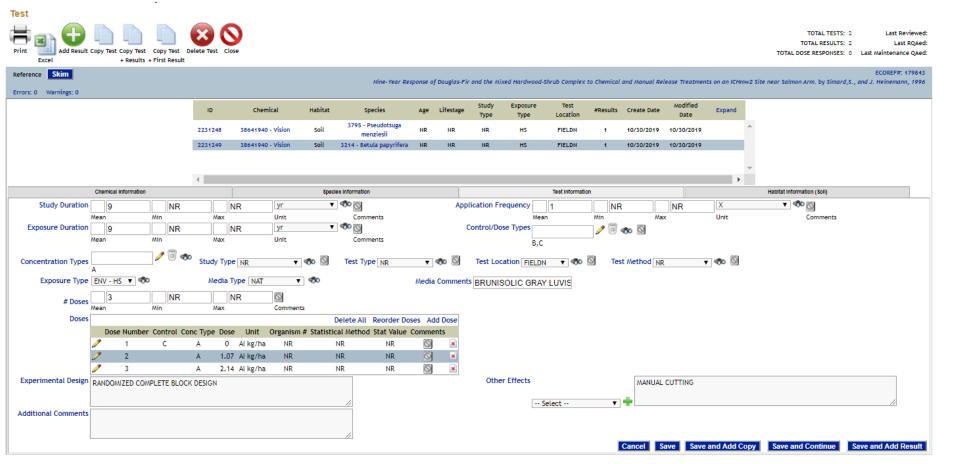
NOEC/NOEL/LOEC/LOEL





<sup>\*</sup> ECOTOX Vocabularies: https://cfpub.epa.gov/ecotox/help.cfm?sub=term-appendix

### **ECOTOX Data Fields**





#### **GUI for data curation**

- Up to 90 entities (300-400 data fields) per study
- Following controlled vocabularies
- Computationally assisted
- Consistent extraction

#### \* ECOTOX Vocabularies:

https://cfpub.epa.gov/ecotox/help.cfm?sub=term-appendix

## Informing Study Evaluation

Regulatory Toxicology and Pharmacology 88 (2017) 227-237



Contents lists available at ScienceDirect

Regulatory Toxicology and Pharmacology

journal homepage: www.elsevier.com/locate/yrtph

Relevance and reliability of experimental data in human health risk assessment of pesticides



#### Toxicology Letters

Volume 189, Issue 2, 10 September 2009, Pages 138-144



"ToxRTool", a new tool to assess the reliability of toxicological data



### Environmental Toxicology and Chemistry

Hazard/Risk Assessment 🗈 Open Access 🕲 📵 🥏

CRED: Criteria for reporting and evaluating ecotoxicity

Caroline T.A. Moermond , Robert Kase, Muris Korkaric, Marlene Ågerstrand

First published: 24 September 2015 | https://doi.org/10.1002/etc.3259 | Citations: 85

### Select study evaluation questions with relevant ECOTOX field(s)

#### Chemical

- Is test substance identified? Required for inclusion in ECOTOX
- Is the purity of test substance reported? **Chemical Purity**
- Were chemical concentrations verified? <u>Chemical Analysis</u> (e.g., nominal versus measured concentrations)

#### **Species**

- Is the species given? Verifiable species (Scientific Name, etc.) required for inclusion in ECOTOX
- Are the organisms well described? <u>Organism Source</u>, <u>Lifestage</u>,
   <u>Age</u>, <u>Gender</u>, <u>Initial</u> and <u>Final Weight</u>

#### Test Conditions

- Are appropriate controls performed? A control is required for inclusion in ECOTOX, type described in Control
- Is a guideline method (e.g., OECD) used? <u>Test Method</u>
- Are the experimental conditions appropriate and acceptable for the test substance and organism? <u>Test Method</u>, <u>Media Type</u>, <u>Test Location</u>, <u>Experimental Design</u>, Physical and Chemical Soil and Water Parameters (e.g., <u>pH</u>, <u>Temperature</u>, <u>Dissolved</u> <u>Oxygen</u>)

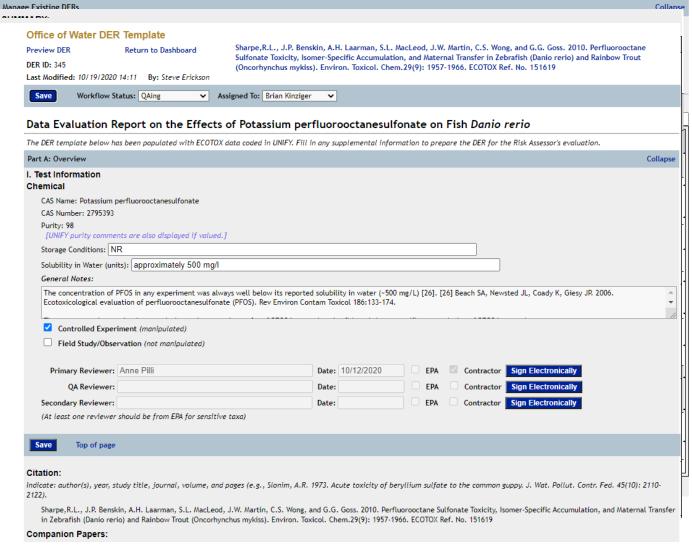
#### **Test Results**

- Are the reported effects and endpoints appropriate for the purpose, test substance and organism? <u>Effect Measurement</u>, <u>Endpoint</u>
- Is the response/effect statistically significant? **Statistical**Significance, Significance Level

### **Developing Data Evaluation Tools**



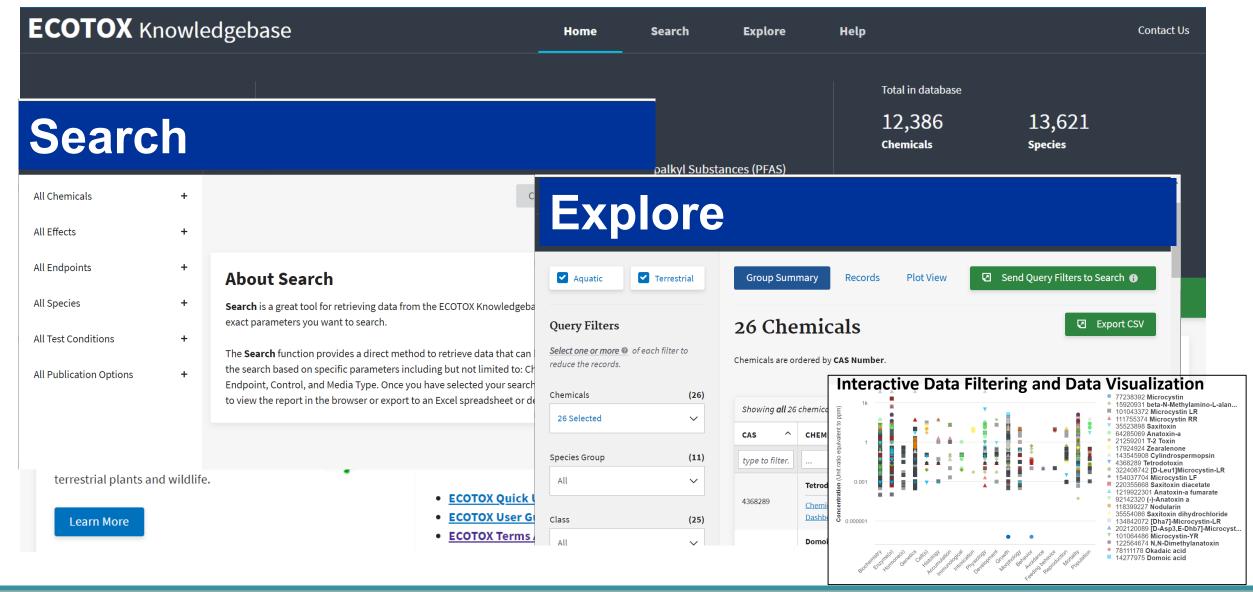
Collaboration with USEPA's Office of Water



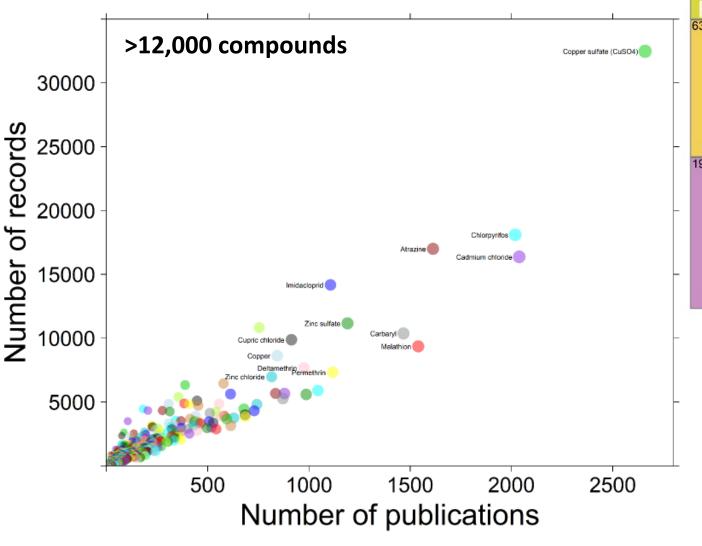
- Application pulls objective data extracted from existing records
- UNIFY platform now has ability for curators to add subjective observations
- Allows multiple reviewers
  - Primary
  - QA
  - Secondary

### **ECOTOX Version 5**

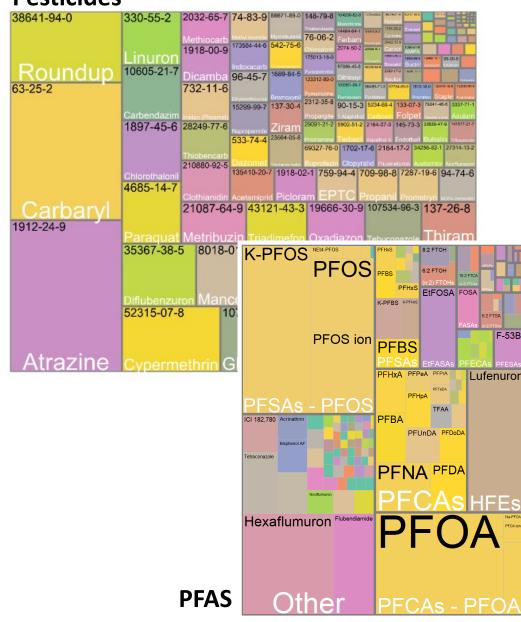
#### www.epa.gov/ecotox



### Chemicals

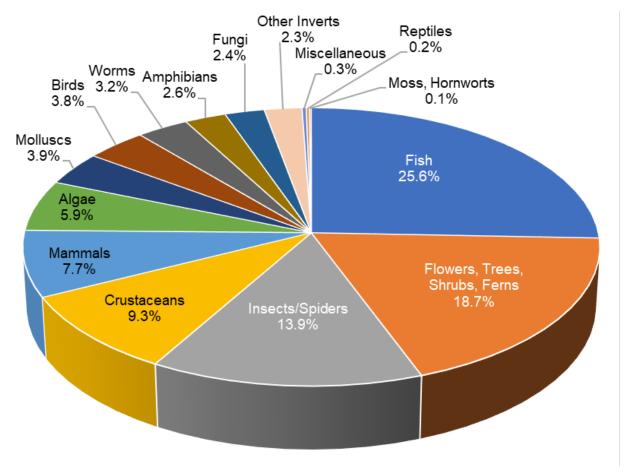


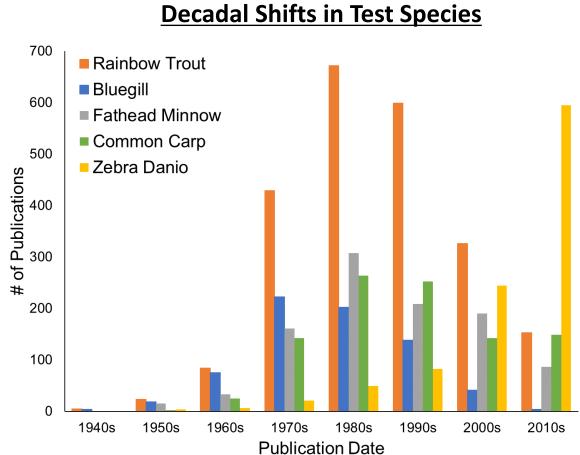
#### **Pesticides**



### **Species** (n = 13,621)

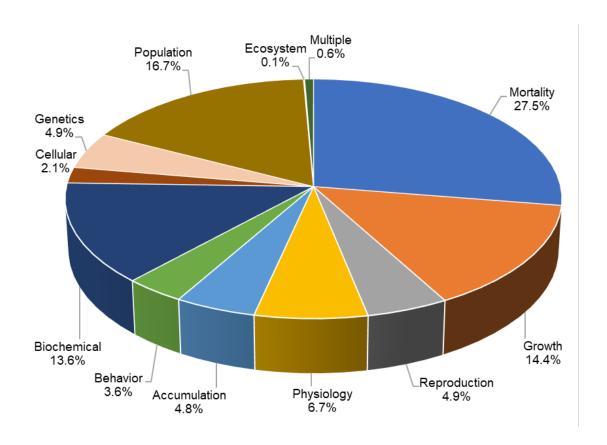
#### % of Records by Species Group (Sept 2021)



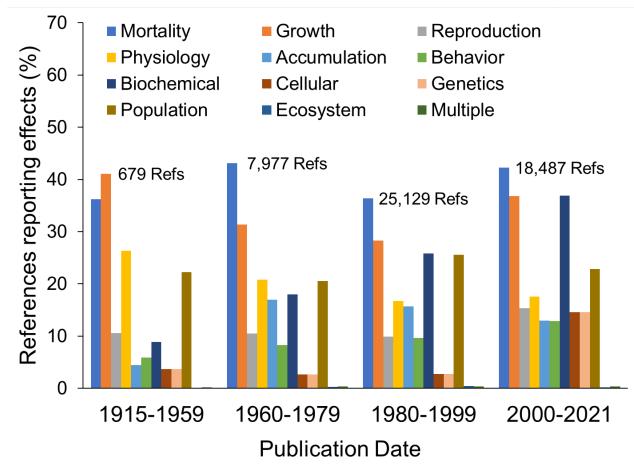


### **Diversity of Effects**

#### % of Records by Effect Group (Sept 2021)

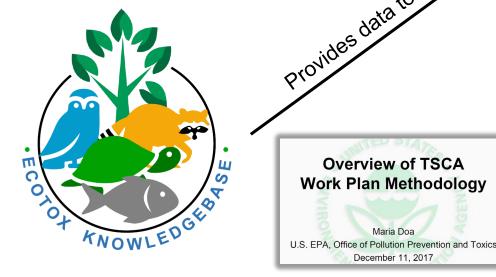


#### **Increases in Biochemical and Genetic Effects Reported**



### **Applications**

Chemical environmental toxicity data for aquatic life, terrestrial plants and wildlife

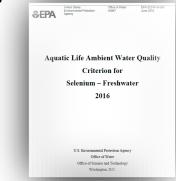


EPA Program Offices and Regions,
States, Tribes, Other Federal Agencies
and International Entities

<u>Ecological Risk Assessment</u> for Office of Pesticides for chemical registration and re-registration (FY20 – 27 chemicals).

Ambient Water Quality Criteria for Aquatic Life

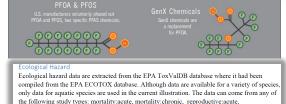
Ecological hazard data for the <u>Prioritization</u> and <u>Assessment of Chemicals</u> for TSCA/Lautenberg Act.





Ecological Site Assessments and in Emergency Response by Office of Land and Emergency Management (Superfund and ORCR), HQ, Regions and States.

<u>Ecological toxicity data for PFAS</u> to researchers, EPA Eco Risk Assessment Forum, DoD Tri-Services ERA Work Group and others.



reproductive:chronic, growth:acute, growth:chronic (all from ECOTOX). The types of effect

levels are LDxx/LCxx/ECxx/EDxx where xx can range from 1% to 100%, and LOEL/NOEL/LOEC/NOEC. Values must be in units of mg/L. For each chemical, the lowest toxicity value was separately determined for acute and chronic studies, regardless of species. Th

### **Applications**

Chemical environmental toxicity data for aquatic life, terrestrial plants and wildlife



Data used for

https://doi.org/10.23645/epa comptox.11971392

Linking environmental contaminant concentrations to potential effects

Identify data gaps, Inform study design, Compare to new toxicity studies

Adverse Outcome Pathway (AOP) development

**EPA Program Offices and Regions, States, Tribes, Other Federal Agencies** and International Entities

#### **Tools and Applications**

**Toxicity Reference Values** (TRVs) and Benchmarks

Species Sensitivity Distributions (e.g., US EPA's SSD Toolbox, Endangered species analyses, U.S. EPA's WebICE, NOAA's CAFE)

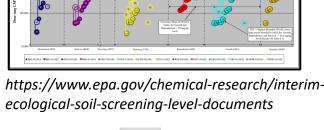
Predicted No Effect Concentrations (PNECs) and

*Eco-TTCs* (e.g., EnviroTox, NORMAN)

**Quantitative Structure-**Activity Relationships and other models



https://gsartoolbox.org



EnviroTox Search Analysis Documentation About https://doi.org/10.1002/etc.4382

PNEC Derivation and EcoTTC Analysis; CTD Analysis



https://www.norman-network.com/nds/ecotox



https://www.epa.gov/tsca-screening-

relationships-ecosar-predictive-model

tools/ecological-structure-activity-

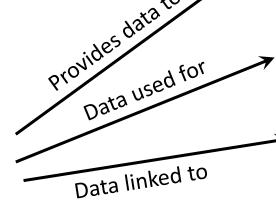
T.E.S.T. (Toxicity **Estimation Software Tool)** 

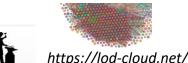
https://www.epa.gov/chemicalresearch/toxicity-estimationsoftware-tool-test

### **Applications**

Chemical environmental toxicity data for aquatic life, terrestrial plants and wildlife







Biological Ontologies\*

http://www.obofoundry.org/

Pathways and Disease Databases\*







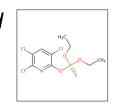
Health & Environmental Research Online (HERO)\* (https://hero.epa.gov/)

EPA Program Offices and Regions, States, Tribes, Other Federal Agencies and International Entities

**Tools and Applications** 

#### **Databases/Resources**

U.S. EPA CompTox Chemicals Dashboard (https://comptox.epa.gov/dashboard/)
OECD eChemPortal (https://www.echemportal.org/echemportal/



Adverse Outcome Pathway Wiki\* (https://aopwiki.org/)



Sequence Alignment to Predict Across Species
Susceptibility (SeqAPASS)\*
(https://doi.org/10.1093/toxsci/kfw119)

\*Future

### **Summary**

- Systematic and transparent procedures to identify and curate ecological toxicity data
- 30 year plus history, with major recent updates and evolution in the near future
  - Maintain comprehensive and quality review of toxicity data
  - Enhance ease of data access and clarity
  - Meet the demands for increased pace of chemical assessments
  - Expand to reflect shifts in toxicity testing paradigm
- Curated data on public website (<u>www.epa.gov/ecotox</u>), readily available for exploration, querying, and export for risk assessments, risk management and research

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### **Acknowledgements and Contact Info**

#### **Jennifer Olker**

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Dale Hoff, GLTED Division Director

Colleen Elonen, SCDCD (previous ECOTOX coordinator)

Contract staff:

General Dynamics Information Technology (GDIT)

SpecPro Professional Services (SPS)

Senior Environmental Employment (SEE) staff

www.epa.gov/ecotox

**ECOTOX Support:** 

218-529-5225

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